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Office of the Solicitor
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Appeal No. 2003-1746

Confirmation No. 2901

Re: U.S. Patent Application Serial No. 09/620,392 filed July 19, 2000
Inventors: Andrey A. BOUKHAROV *et al.*
Title: Plant Genome Sequence and Uses Thereof
Atty. Dkt: 16517.112

Sir:

Transmitted herewith for appropriate action by the U.S. Patent and Trademark Office, is an original Petition for Review to the United States Court of Appeals for the Federal Circuit. Three copies of this Petition, as well as Arnold & Porter LLP Check No. 203305 in the amount of $250.00, are being hand-carried, on even date, to the Court of Appeals for the Federal Circuit.

It is not believed that any additional fees are due in conjunction with this filing. However, if any fees are required in the present application, including any fees for extensions of time, then the Commissioner is hereby authorized to charge such fees to Arnold & Porter LLP Deposit Account No. 50-2387, referencing docket number 16517.112.

Sincerely,

David R. Marsh (Reg. No. 41,408)

Enclosure

**UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT**

Andrey A. BOUKHAROV *et al.*, Petitioner

v. PETITION FOR REVIEW

United States Patent and Trademark Office, Respondent.

Andrey A. Boukharov, Yongwei Cao, David K. Kovalic, Jingdong Liu, James McIninch, and Wei Wu hereby appeal to the Court of Appeals for the Federal Circuit for review of the decision of the Board of Patent Appeals and Interferences ("B.P.A.I."), U.S. Patent and Trademark Office, entered on June 30, 2004 in application serial number 09/620,392 filed July 19, 2000 (also accorded B.P.A.I. appeal number 2003-1746).

Dated: August 27, 2004

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Paper No. 35

# UNITED STATES PATENT AND TRADEMARK OFFICE

## BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte AUDREY A. BOUKHAROV, YONGWEI CAO, DAVID K. KOLAVIC, JINGDONG LIU, JAMES McININCH, and WEI WU

Appeal No. 2003-1746
Application No. 09/620,392

HEARD June 8, 2004

Before WILLIAM F. SMITH, ADAMS, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

## DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-4, 6-9, and 16-20, all of the claims remaining. Claims 1 and 2 are representative and read as follows:

1. A substantially purified nucleic acid molecule having a nucleic acid sequence of SEQ ID NO: 1 or complement thereof.

2. A substantially purified nucleic acid molecule comprising a fragment nucleic acid sequence having from about 50 to about 100 nucleotide residues; wherein said fragment nucleic acid sequence exhibits complete complementarily to a second nucleic acid molecule having a nucleic acid sequence of SEQ ID NO: 1 or complement thereof.

The examiner does not rely on any prior art.

Claims 1-4, 6-9, and 16-20 stand rejected under 35 U.S.C. §§ 101 and 112, first paragraph, as lacking patentable utility.

Claims 1-4, 6-9, and 16-20 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description.[1]

We affirm the utility rejections and reverse the description rejection.

Background

The subject matter of the present appeal is directed to "genomic DNA sequences from Oryza sativa (rice) plants." More specifically, the "invention provides a substantially purified nucleic acid molecule, the nucleic acid molecule capable of specifically hybridizing to a second nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:1 through SEQ ID NO:69652 or complements thereof or fragments of either."

According to the specification,

> [a] subset of the nucleic acid molecules of the present invention includes nucleic acid molecules that are marker molecules. Another subset of the nucleic [acid] molecules of the present invention includes nucleic acid molecules that are promoters and/or regulatory elements. Another subset of the nucleic acid molecules of the present invention includes nucleic acid molecules that encode a gene or fragment thereof. Another subset of the nucleic acid molecules of the present invention encodes proteins or fragments of proteins.

Page 17. The specification provides no further guidance on which of the 69,652 disclosed sequences fall into each of these subsets.

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[1] The examiner's statement of the rejection actually speaks in terms of lack of enablement. See the Examiner's Answer, page 5 (The claims "contain[] subject matter which lacks written description in the specification in such a way as to enable one skilled in the art . . . to make and/or use the invention."). The

The originally filed claims encompassed all of the 69,652 disclosed sequences. See, e.g., original claim 1 (specification, page 55,578).[2] On June 18, 2001 (Paper No. 7), the examiner entered a restriction requirement into the record, requiring appellants to elect, inter alia, a single nucleotide sequence for examination on the merits. Paper No. 7, page 2. In response, Appellants elected SEQ ID NO:1. See Paper No. 8, received July 17, 2001.

The disclosure that relates specifically to SEQ ID NO:1 is found in the specification's Table 1 and reads as follows, in its entirety:

| | | | |
|---|---|---|---|
| Seq No. | 1 | Seq. ID | OJ990503_31.9819.C2 |
| Gene No. | 1 | Strand | - |
| Start | 397 | End | 1864 |
| Name | OJ990503_31.9819.C2.o1.gs | Method: | GENSCAN |
| Start | 397 | End | 1238 |
| GI | none | Score | .93 |
| Exons | 397. . 591, 879. . 1238 | | |

| | | | |
|---|---|---|---|
| Seq No. | 1 | Seq. ID | OJ990503_31.9819.C2 |
| Gene No. | 1 | Strand | - |
| Start | 397 | End | 1864 |
| Name | OJ990503_31.9819.C2.o1.tm | Method: | TBLASTX:Maize |
| Start | 1017 | End | 1864 |
| GI | none | Score | 150 |
| Exons | 1017. . 1250, 1018. . 1245, 1020. . 1247, 1243. . 1296, 1249. . 1296, 1377. . 1418, 1382. . 1420, 1532. . 1600, 1534. . 1596, 1706. . 1735, 1745. . 1864 | | |

Page 104.

The specification sets forth a number of utilities for the claimed nucleic acid molecule which are characterized by the examiner as "[g]eneric to any rice nucleic acid

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examiner's reasoning, however, explains the rejection in terms of lack of written description. We understand the rejection to be based on the written description requirement of § 112.

[2] The record is unclear as to precisely how many pages are in the specification. According to an error sheet generated by the USPTO's Office of Initial Patent Examination, the specification contains 68,885 pages; according to Appellants' page numbering, it contains "only" 55,580 pages. We have not attempted to resolve this discrepancy since it does not affect the issues on appeal.

sequences." Examiner's Answer, page 4. The examiner concluded that these uses do not establish patentable utility:

> The claimed nucleic acids are not supported by a specific asserted utility because the disclosed uses of these nucleic acids are generally applicable to rice genomic nucleic acid. The specification states that the nucleic acid compounds are useful for gene mapping, marker assisted introgress[i]on of traits, physical mapping, etc. (page 9 and 49). All these possible uses are generic to rice any nucleic acid sequences. Further, the claimed nucleic acids are not supported by a substantial utility. . . . Identifying and studying the properties of a protein itself or the mechanisms in which the protein is involved does not define a "real world" context of use. Similarly, the other listed and asserted utilities as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds.

Examiner's Answer, pages 3-4.

In presenting their case on appeal, appellants focus on use of the claimed nucleic acid molecules to identify the presence or absence of a polymorphism, and their use as probes or as a source for primers. See the Appeal Brief, pages 6-13. According to Appellants, "they have disclosed nucleic acid molecules which, in their current form, provide at least one specific benefit to the public, for example, the ability to identify the presence or absence of a polymorphism in a population of rice plants." Id., page 4. Furthermore, appellants assert, "[t]he specification discloses that the claimed nucleic acid molecules can be used . . . to isolate nucleic acid molecules of other plants and organisms." Id., page 9.

1. Claim construction

The claims stand or fall together. Appeal Brief, page 3. Claim 2 is the broadest claim on appeal and we will consider it as representative.

As set forth above, claim 2 is directed to a "substantially purified" nucleic acid molecule that comprises a "fragment nucleic acid sequence having from about 50 to about 100 nucleotide residues"; where the 50-100 nucleotide sequence "exhibits complete complementarity to a second nucleic acid molecule having a nucleic acid sequence of SEQ ID NO:1" or its complement.

The specification defines "substantially purified" to mean

> a molecule separated from substantially all other molecules normally associated with it in its native state. More preferably a substantially purified molecule is the predominant species present in a preparation. A substantially purified molecule may be greater than 60% free, preferably 75% free, more preferably 90% free, and most preferably 95% free from the other molecules (exclusive of solvent) present in the natural mixture. The term "substantially purified" is not intended to encompass molecules present in their native state.

Page 16, lines 12-18. As we understand the claimed invention, the use of the transitional term "comprising" does not allow for internal alterations (e.g., insertions or deletions) of the "fragment nucleic acid sequence" recited in the claim, but instead only allows for the addition of nucleotides or other molecules at either end of that sequence. Thus, claim 2 encompasses, inter alia, genes and fragments thereof, full or partial open reading frames, fusion constructs, and cDNAs.

Accordingly, we interpret claim 2 as directed to a nucleic acid molecule, separated from substantially all other molecules normally associated with it in its native state, that includes at least about 50 nucleotides that are completely complementary to a part of SEQ ID NO:1 or to the complement of a part of SEQ ID NO:1.

2. Utility

The starting point for determining whether the claimed nucleic acid molecules possess utility under 35 U.S.C. § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). At issue in Brenner was a claim to "a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced." Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that "where a claimed process produces a known product it is not necessary to show utility for the product." Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be "useful," that "simple, everyday word can be pregnant with ambiguity when applied to the facts of life." Id. at 529, 148 USPQ at 693. Thus,

> [i]t is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the "new and useful" phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man's grasp and where little or nothing is wholly beyond the pale of "utility"—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.[3]

[3] The invention at issue in Brenner was a process, but the Court expressly noted that its holding "would apply equally to the patenting of the product produced by the process." Id. at 535, 148 USPQ at 695-96.

The Court, finding "no specific assistance in the legislative materials underlying § 101," based its analysis on "the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other." Id. at 532, 148 USPQ at 695. The Court concluded that "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Id. at 534-35, 148 USPQ at 695.

The Court considered and rejected the applicant's argument that attenuating the requirement of utility "would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge." The Court noted that, while there is value to encouraging disclosure, "a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development." Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not "mean to disparage the importance of contributions to the fund of scientific information short of the invention of something 'useful,'" and that it was not "blind to the prospect that what now seems without 'use' may tomorrow command the grateful attention of the public." Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of § 101's utility requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroidal research and in the application of steroidal materials to veterinary or medical practice." Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." Id. at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the first instance whether the

compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are." Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. "There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher' was recognized, and clearly rejected, by the Supreme Court" in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. "In the German application, Ziegler disclosed only that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was 'plastic-like.'" Id. at 1203, 26 USPQ2d at 1605. "Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility." Id. The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a rejection based on an intervening reference. Id. "[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of the German application; but in that application Ziegler had not yet gotten there." Id.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were "well recognized in the art as valuable for use in cancer chemotherapy." Id., 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court noted that the data derived from the mouse model were "relevant to the treatment of humans and [were] not to be disregarded," id. at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that "[it] is axiomatic that an invention cannot be considered 'useful,' in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious." Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court "perceive[d] no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question." Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by

"marshal[ling] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds ..., analogous to the benefit provided by the showing of an in vivo utility." Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The specification disclosed that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at 1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use" that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy §

101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk, 376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best ... on the way to discovering a practical utility for polypropylene at the time of the filing," but not yet there. Ziegler, at 1203, 26 USPQ2d at 1605.

With these principles in mind we turn to the issues at hand. Of the many utilities asserted in the specification, two have received the most attention in the briefing in this appeal; i.e., identification and detection of polymorphisms and use as probes or as a source for primers. We will focus on these asserted utilities first.

a. Polymorphisms

This utility is discussed at pages 57-64 of the specification in terms of what polymorphisms are and how one would go about determining the existence of a polymorphism. The discussion in this portion of the specification, however, is not specific to SEQ ID NO:1. To the contrary, according to the specification, "[t]he [69,652] nucleic acid molecules of the present invention can be used to identify polymorphisms. In one embodiment, one or more of the nucleic acid molecules . . . may be employed as a marker nucleic acid molecule to identify . . . polymorphism(s)." Page 57. The specification does not explain why any particular one of the 69,652 nucleotide molecules disclosed in the specification, or more specifically SEQ ID NO:1, would in fact be useful in detecting polymorphisms.

Rather, Appellants argue that "the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usually demonstrates that the two (or more) populations being compared share a common genetic heritage." Appeal Brief, page 9. In other words, Appellants' position is that a rice genomic DNA by definition possesses patentable utility because it can be used by itself in determining whether populations share a common genetic heritage. While that may be a "utility," we do not find that it is a substantial utility.

Without knowing any further information in regard to the gene represented by a nucleotide sequence, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage. As the examiner explains,

> [a] "polymorphism" is a collective concept defined by at least two variants (or alleles) found within members of a species collectively. Thus, one detects the presence of a polymorphism by analyzing multiple members of the species, i.e. analyzing a population. . . . The specification fails to disclose a specific and substantial utility for the claimed invention in the capacity of detecting polymorphisms, because it does not disclose whether the claimed nucleic acid molecules can, in fact, be used to detect any polymorphism whatsoever. . . .
>
> The specification generally teaches using the claimed polynucleotides to identify a polymorphism, but fails to teach that a polymorphism could in fact be detected, or a specific polymorphism that could be detected. The specification generally teaches using a polymorphism, detectable with the claimed nucleic acid molecules, as a molecular marker for a linked trait of interest, but fails to teach either the polymorphism or the trait of interest.

Examiner's Answer, pages 12-13. In contrast, at the other end of the "utility spectrum" would be information gleaned from detecting the presence or absence of a polymorphism when it is known what effect the gene represented by the claimed sequence has in the development and/or phenotype of the plant. Somewhere between having no knowledge (the present circumstances) and having complete knowledge of the gene and its role in the plant's development and/or phenotype lies the line that defines "substantial utility." We need not draw the line or further define it in this case because the facts in this case represent the lowest end of the spectrum, i.e., an insubstantial use.

b. Probes or source of primers

Appellants argue that the "specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms." Appeal Brief, page 9. That may be true, but it does not show the patentable utility of the claimed nucleic acids, because the nucleic acids isolated from other plants have no apparent, substantial use. Again, the present specification does not attribute any property in terms of plant trait or phenotype to SEQ ID NO:1. In the absence of such information, nucleic acids from other plants that hybridize to the claimed nucleic acids, themselves lack substantial utility. Thus, the use of the claimed nucleic acids to isolate such nucleic acids does not represent a substantial utility.

Appellants also assert that the claimed nucleic acid molecules may be used in a "chromosome walk." Appeal Brief, pages 10-11. According to Appellants,

> [t]he claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate a promoter that is active in Oryza sativa. A random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter. Furthermore, even if a random nucleic acid provided a better starting point than the claimed nucleic acid molecules, it would not obviate the utility of the claimed nucleic acid molecules.

Id., page 10. As we understand it, Appellants' argument is that the claimed nucleic acids may be useful in searching for promoters that are active in rice tissues.

The specification, however, fails to demonstrate that the nucleic acid represented by SEQ ID NO:1 would be useful in obtaining a successful result from such a search. The specification states that "[a]nother class of agents of the present invention are nucleic acid molecules having promoter regions or partial promoter regions within SEQ ID NO:1 through SEQ ID NO:69652." Page 27.

> Promoters . . . include, but are not limited to, oxygen responsive cis elements . . ., light regulatory elements . . ., elements responsive to gibberellin . . ., elements responsive to abscisic acid . . ., elements similar to abscisic acid responsive elements . . ., auxin responsive elements . . ., ethylene responsive cis elements . . ., sucrose responsive elements . . ., heat shock response elements . . ., Elicitor responsive elements . . ., drought responsive elements . . ., light-independent regulatory elements . . ., ACGT elements . . ., [and] prolamin box elements.

Pages 28-32.

The specification does not provide any expectation of successfully using any of the 69,652 nucleic acid molecules disclosed in the specification, or more specifically the nucleic acid of SEQ ID NO:1, to isolate any of the promoters exhaustively listed in the specification, or any other promoter. Even if SEQ ID NO:1 represents a gene that is expressed in rice tissue, the specification provides no characterization of its expression (e.g., amount expressed, timing of expression, tissues in which or conditions under which it is expressed) that would suggest a utility for its putative promoter.

It is true, as Appellants argue, that "[a]n invention may be 'less effective than existing devices but nevertheless meet the statutory criteria for patentability.'" Appeal Brief, page 11. However, with Appellants' claimed invention, there is no evidence or expectation that the claimed nucleic acid molecules would be "effective" at all. An invention does not have utility sufficient to satisfy § 101 until it is "refined and developed" to the point of providing a specific benefit in currently available form. See Brenner, 383 U.S. at 534, 148 USPQ at 695.

Appellants argue that the claimed nucleotide sequences are no less useful just because other nucleic acids can also be used to isolate promoters. See the Appeal Brief, page 10: "[T]he Examiner suggests that the asserted utilities are legally

insufficient simply because other molecules can be used for the same purpose. This position is wrong as a matter of law – there is no requirement of exclusive utility in the patent law."

This argument is not persuasive. Appellants have not been asked to identify a utility that is unique, i.e., not shared by any other compounds or compositions. Rather, Appellants have been required to identify a utility that is specific to the invention claimed, as opposed to one that would apply regardless of the specific properties of the claimed invention. See, e.g., Brenner, 383 U.S. at 534, 148 USPQ at 695 (An invention does not have utility sufficient to satisfy § 101 until it is "refined and developed" to the point of providing a specific benefit in currently available form.).

An invention certainly can have a utility that is shared by other compounds or compositions. Take, for example, an application that claims ibuprofen and discloses that it is useful as an analgesic. No one would argue that a claim to ibuprofen lacks utility simply because aspirin and acetaminophen are also useful as analgesics. On the other hand, not every utility will satisfy § 101, even if the utility is shared by a class of inventions. Assume that the above-described application did not disclose that ibuprofen was an analgesic but only disclosed that it is useful because it can be used to fill a jar, which would then be useful as a paperweight. There would be little doubt that this disclosed utility would not satisfy § 101, even though the utility is shared by a large class of inventions, viz., those whose physical embodiments have mass. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101.

c. Other arguments

Appellants argue that the specification "discloses additional utilities for the claimed nucleic acid molecules, including introduction of the claimed nucleic acid molecules into a plant or plant cell (either as sense or antisense inhibitors), which can then be used to screen for compounds such as a herbicide." Appeal Brief, page 6 (footnote omitted). Specifically, Appellants argue (id.) that "a compound can be provided to both an antisense plant and a control plant (no antisense) and the effect of the compound on the plant can be monitored." Appellants analogize this proposed procedure to a "cell-based assay" which, they assert, has a "legally sufficient utility." Id.

Suffice it to say that an otherwise uncharacterized nucleic acid molecule is being claimed in this application, not an assay. The portions of the specification cited in support of this argument (pages 69 and 86-88) indicate that the nucleic acid molecule must be introduced into a plant cell and transcribed using an appropriate promoter to result in either expression of the protein or suppression of an endogenous protein. The specification does not indicate that such a method is feasible when the nucleic acid to be used is uncharacterized as here. Such a use does not provide a specific or substantial benefit in currently available form.

Appellants also argue that the claimed nucleic acids are useful to measure the level of mRNA in a sample through use of microarray technology and use as molecular markers. Appeal Brief, page 7. In regard to microarrays, appellants argue (id., n.3) that it is "standard practice" to screen populations of nucleic acids with EST sequences without characterizing each and every target mRNA. We find that the asserted utility of the claimed nucleic acid—as one component of an assay for monitoring gene

expression—does not satisfy the utility requirement of § 101. Such a use does not provide a specific benefit in currently available form.

We accept, for argument's sake, that a person skilled in the art could use the claimed nucleic acid, in combination with other nucleic acids, to monitor changes in expression of the gene that encompasses the nucleic acid depicted in SEQ ID NO:1. However, the specification provides no guidance that would allow a skilled artisan to use data relating to expression of such a gene in any practical way. The specification provides no guidance regarding what the SEQ ID NO:1-specific information derived from a gene expression experiment would mean. As the examiner points out, "further experimentation is required to identify a 'real world use.' . . . A positive result to such a screen requires further experimentation to determine what, if anything, such a change means." Examiner's Answer, pages 8-9.

To highlight the examiner's assertion, suppose, for example, that a researcher found that SEQ ID NO:1 expression was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. Maybe the meaning in a change in SEQ ID NO:1 expression would depend on other factors, but again the specification provides no hint as to what other factors might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), or the degree of increase? The specification provides no guidance as to how to interpret the results that might be seen using SEQ ID NO:1 in a gene expression assay.

In effect, Appellants' position is that the claimed nucleic acids are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. We do not agree that such a disclosure provides a "specific benefit in currently available form." Rather, the present case seems analogous to Brenner. In Brenner, the applicant claimed a method of making a compound but disclosed no utility for the compound. 383 U.S. at 529, 148 USPQ at 693. The Court held that a process lacks utility if it produces a product that lacks utility. Id. at 534, 148 USPQ at 695. Here, Appellants claim a product asserted to be useful in a method of generating gene-expression data, but the specification does not disclose how to interpret those data. Just as the process claimed in Brenner lacked utility because the specification did not disclose how to use the end-product, the products claimed here lack utility, based on their use in gene expression assays, because the specification does not disclose how to use gene expression data pertaining to SEQ ID NO:1.

In addition, assuming arguendo that a generic gene expression assay—one based on monitoring expression of a collection of uncharacterized nucleic acids—would provide a useful tool for, e.g., drug discovery, it does not follow that each of the nucleic acids in the assay necessarily has patentable utility. Although each nucleic acid in the assay contributes to the data generated by the assay overall, the contribution of a single nucleic acid—its data point—is only a tiny contribution to the overall picture.

The Brenner Court held that § 101 sets more than a de minimis standard for utility. Therefore, the patentable utility of a gene expression assay, for example, does not necessarily mean that each tiny component of the assay also has patentable utility.

A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities. Each claimed invention must be shown to meet § 101's utility requirement in order to be patentable; it must provide a specific benefit in currently available form. Providing a single data point among thousands, even if the thousands of data points collectively are useful, does not meet this standard.

We also conclude that § 101's utility requirement is not satisfied by Appellants' assertion that the claimed nucleic acid molecules are useful as molecular markers or probes. Again, using one of the claimed nucleic acids as a molecular marker or probe to hybridize to part of a rice chromosome merely generates a single, uncharacterized data point that is useful only when combined with thousands of other data points. For the reasons discussed above in regard to gene expression assays, such uses do not represent "substantial" utility, as required by Brenner.

Appellants argue that ESTs (and presumably other uncharacterized nucleic acids; the claims on appeal are not directed to ESTs) have real world value as seen from the "growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs." Appeal Brief, page 12. Since Appellants fail to provide any suggestion on which use of ESTs this industry is premised on, we can only assume that Appellants are referring to the potential usefulness of EST databases, clone sets, or microarrays. The claims on appeal, however, are not directed to EST databases, clone sets, or microarrays, but to individual, uncharacterized nucleic acids. Again, we do not agree that the one data point which may be provided by using the uncharacterized nucleic acid molecules of the claims in such devices represents a substantial use.

In addition, it is reasonable to expect that the rule Appellants proffer – that uncharacterized nucleic acids are individually patentable because they are useful in gene expression assays – would hurt, rather than help, what they characterize as a "multi-million dollar industry in the United States premised on the usefulness of ESTs." Under Appellants' standard, any uncharacterized nucleic acid from most (if not all) organisms would be held to have patentable utility based on its use in generating gene expression data.[4] The practical effect of this standard would be that making a microarray with, e.g., 1000 genes represented on it would require investigating all of the oligonucleotides on the microarray to ensure that they were not the subject of someone else's patent.

For each of the genes or polypeptides (or fragments thereof) that was the subject of a patent claim held by someone else, a license would have to be negotiated – potentially thousands of such negotiations for the finished product. These transaction costs would have to be incurred for each new product that an aspiring microarray manufacturer wished to market. The industry gridlock likely to result from this scenario has been termed a "tragedy of the anticommons":[5]

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[4] We can take judicial notice of the fact that other organisms are of interest for many different reasons, such that gene expression assays could conceivably be used in their research. Humans, of course, are of interest in medical research. Other organisms are of interest to researchers because they have been historically well-studied (e.g., yeast, Arabidopsis, Drosophila), or because they are used as animal models for testing pharmaceuticals (e.g., mice, chimpanzees, rabbits), or because they are commercially valuable (e.g., pigs, corn, tomatoes), or because they are pests (e.g., Fusarium, ragweed, corn borers, zebra mussels), or because they are pathogens (e.g., Candida, various bacteria, tapeworms).

[5] Heller et al., "Can patents deter innovation? The anticommons in biomedical research," Science, Vol. 280, pp. 698-701 (1998). Available online at www.sciencemag.org/cgi/content/full/280/5364/698.

> By conferring monopolies in discoveries, patents necessarily increase prices and restrict use—a cost society pays to motivate invention and disclosure. The tragedy of the anticommons refers to the more complex obstacles that arise when a user needs access to multiple patented inputs to create a single useful product. Each upstream patent allows its owner to set up another tollbooth on the road to product development, adding to the cost and slowing the pace of downstream biomedical innovation.

Heller, page 698.

The Supreme Court has warned against allowing too many tollbooths on the road to innovation:

> Patents . . . are meant to encourage invention by rewarding the inventor with the right, limited to a term of years fixed by the patent, to exclude others from the use of his invention. . . . But in rewarding useful invention, the "rights and welfare of the community must be fairly dealt with and effectually guarded." Kendall v. Winsor, 21 How. 322, 329 (1859). . . . To begin with, a genuine "invention" or "discovery" must be demonstrated "lest in the constant demand for new appliances the heavy hand of tribute be laid on each slight technological advance in an art."

Sears, Roebuck & Co. v. Stiffel Co., 376 U.S. 225, 230, 140 USPQ 524, 527 (1964).

The basic quid pro quo of the patent system requires disclosure of an invention having substantial utility. Appellants' disclosure in this case does not provide a specific benefit in currently available form, and therefore lacks the substantial utility required by 35 U.S.C. § 101. We therefore affirm the rejection of claim 2 under 35 U.S.C. § 101. Claims 1, 3, 4, 6-9, and 16-20 with claim 2.

3. Enablement

The examiner rejected claims 1-4, 6-9, and 16-20 under 35 U.S.C. § 112, first paragraph, on the basis that "since the claimed invention . . . due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility for the reasons set forth above, one skilled in the art clearly would not

know how to use the claimed invention." Examiner's Answer, page 4. This rejection is simply a corollary of the finding of lack of utility.

Appellants argue that "[t]his rejection . . . has been overcome by the arguments stated above regarding utility." Appeal Brief, page 14. We do not agree that Appellants' arguments overcome the rejection for lack of utility. Thus, our conclusion with respect to the § 101 issue also applies to the nonenablement rejection. On this basis we affirm the rejection of claims 1-4, 6-9, and 16-20 under the enablement provision of 35 U.S.C. § 112, first paragraph.

4. Written description

The examiner rejected claims 1-4, 6-9, and 16-20 under 35 U.S.C. § 112, first paragraph, for lack of adequate written description, reasoning that

> [c]laims 1-4, 6-9, and 16-20 are directed to nucleic acids comprising . . . SEQ ID NO:1, or fragments thereof. . . . [G]iven the broad scope of the claims, they are drawn to a genus: any polynucleotide or nucleic acid that minimally contains the sequence of the claimed SEQ ID NO, or a fragment thereof, including any full length gene which contains the sequence. . . . Since the claimed genus encompasses species yet to be discovered, the mere disclosure of a species: sequence of the claimed SEQ ID NO, does not provide an adequate description of the claimed genus. . . . With the exception of SEQ ID NO:1, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotide.

Examiner's Answer, page 5.

As we understand it, the basis of the examiner's rejection is that because of the transitional phrase "comprising", the claims encompass a large genus of nucleic acid molecules which are not adequately described by SEQ ID NO:1. See the Examiner's Answer, pages 18-20. Apparently, the examiner is of the opinion that the claimed

invention should be limited to the nucleic acid molecules set forth in the recited SEQ ID NOs.

In response, Appellants argue that "[t]he fact that the claims at issue are intended to cover molecules that include the recited sequences joined with additional sequences . . . does not mean that Applicants were any less in possession of the claimed nucleic acid molecules." Appeal Brief, pages 15-16.

We have interpreted claim 2 to allow for the addition of nucleotides or other molecules at either end of the recited nucleotide sequences, but not to allow for internal alterations (e.g. insertions or deletions) of the nucleotide sequence SEQ ID NO:1. See pages 4-5, supra. We agree with Appellants that the claims, as we have interpreted them, are supported by an adequate written description in the specification. The fact that the claimed nucleic acid molecules may have other molecules attached to either or both of their 5' or 3' ends does not diminish Appellants' adequate written description of the nucleic acids molecules with the sequences set forth in the recited SEQ ID NOs, as claimed.

Accordingly, we reverse the rejection of claims 1-4, 6-9, and 16-20 for lack of adequate written description.

Summary

Although we reverse the examiner's rejection for lack of adequate written description, we affirm the rejection of claims 1-4, 6-9, and 16-20 for lack of patentable utility.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

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|---|---|
| WILLIAM F. SMITH<br>Administrative Patent Judge | )<br>)<br>) |
| DONALD E. ADAMS<br>Administrative Patent Judge | ) BOARD OF PATENT<br>)<br>) APPEALS AND<br>) |
| ERIC GRIMES<br>Administrative Patent Judge | ) INTERFERENCES<br>)<br>) |

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